REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

I. Amendments to the Specification

The specification is amended to correct a clerical error in paragraph [0023], relating to the amount of protein used in dose B. Support for the correction is found in Figures 1 and 2 of the specification as filed, which both indicate that 30 μg of NY-ESO-1 protein was used for dose B.

II. Claim Amendments

Claim 20 is amended to recite methods comprising administering an amount of a composition containing full length NY-ESO-1 protein and a saponin based adjuvant that is sufficient to reduce the risk of relapse, wherein the ratio of NY-ESO-1 protein to saponin based adjuvant is about 1:1 by weight. This subject matter is supported in Example 1, which reports the use of compositions comprising NY-ESO-1 protein and saponin based adjuvant (ISCOM) in a ratio of about 1:1 by weight (e.g., 10 μg : 12 μg (dose A); 30 μg : 36 μg (dose B), and 100 μg : 120 μg (dose C)).

Applicant notes with appreciation the indication that the previous amendments to claim 20 would be entered after final. Applicant respectfully urges entry of this further amendment after final because it is not believed to raise any new issues or require a further search, and directly addresses one of the stated reasons for maintaining the prior art rejections. Thus, the amendment is believed to place the application in condition for allowance or, at the very least, in better condition for appeal.

Upon entry of this amendment, claims 20-22, 25, 26 and 34-37 will remain pending. These claims are presented for reconsideration.

III. § 102 Rejection

The claims remain rejected under 35 U.S.C. § 102(b) for allegedly being anticipated by Cebon *et al.*, *Proc. Amer. Soc. Clin. Oncol.* 21, abstract 86 (June 2002) ("Cebon"). Office Action, at 2-4. Applicant respectfully traverses.

As reflected in independent claim 20, the instant claims are directed to a method for reducing the risk of relapse in a subject at risk of relapse of a cancer, the cells of which express NY-ESO-1, comprising administering to said subject an amount of a composition containing full length NY-ESO-1 protein and a saponin based adjuvant in a ratio of about 1:1 by weight, sufficient to induce an antibody response to NY-ESO-1 in said subject and reduce the risk of relapse.

As explained previously, the cited Cebon abstract does not teach or suggest that a composition containing full length NY-ESO-1 protein and a saponin based adjuvant is able to ***reduce the risk of relapse*** of cancer ***at any dose***. Thus, the Cebon abstract does not describe the claimed invention, or provide any reasonable expectation that administering a composition comprising full length NY-ESO-1 protein and a saponin based adjuvant would be effective to reduce the risk of relapse.

As also explained previously, the cited Cebon abstract does not indicate the amount of ISCOM that was used with the described doses of NY-ESO-1 protein. Thus, the Cebon abstract does not even enable methods of achieving the results it reports, because the skilled artisan seeking to induce the reported "high titre humoral and cellular immune responses" would not know how much ISCOM adjuvant is required to achieve such results. Of course, since Cebon does not even suggest that its compositions might be effective to reduce the risk of relapse, it falls even further short of enabling methods of reducing the risk of relapse.

In the Advisory Action, the examiner notes that the previously pending claims did not recite an amount of NY-ESO-1 protein or saponin based adjuvant. Applicant does not agree that the claims need to recite specific amounts to overcome the § 102 rejection, because the recitation of an "amount . . . sufficient to . . . reduce the risk of relapse" already distinguishes Cebon, for the reasons outlined above and explained in the previous response. Nevertheless,

in order to advance prosecution, Applicant has amended the claims to recite that the administered composition contains "full length NY-ESO-1 protein and a saponin based adjuvant in a ratio of about 1:1 by weight." Because Cebon does not disclose the amounts of ISCOM used with its doses of NY-ESO-1 protein, it does not teach every aspect of the claimed invention as required for a § 102 rejection.

For at least these reasons, Applicant respectfully urges reconsideration and withdrawal of the anticipation rejection based on Cebon.

IV. § 103 Rejections

The claims remain rejected under 35 U.S.C. § 103 for allegedly being obvious in view of (A) WO 98/14464 in view of Batchu (2003) and WO 03/076455; (B) WO 98/14464, Batchu, and WO 03/076455, further in view of Jager (2000) and U.S. 6,506,386; and (C) Cebon, Jager, WO 03/076455 and "an admission in the specification." Applicant addresses these maintained rejections in turn below.

A. WO 98/14464, Batchu (2003) & WO 03/076455

Claims 20-22, 34 and 35 remain rejected over the combination of WO 98/14464, Batchu and WO 03/076455. Applicant respectfully traverses this rejection.

The Advisory Action maintains this rejection because "Batchu teaches that NY-ESO-1 based therapies can be used . . . to reduce the risk of relapse," but does not provide any citation to support this assertion. As explained previously, Batchu notes that immunotherapeutic approaches using NY-ESO-1 modfied DCs are being ***investigated*** to prevent relapse of aggressive myeloma after chemotherapy ("Discussion," page 1341), but does not teach that its transduced DCs are in fact useful to prevent relapse. Moreover, Batchu provides no indication that a composition comprising NY-ESO-1 and a saponin based adjuvant, rather than NY-ESO-1-modified DCs, would be useful to prevent relapse. Indeed, the assertion that Batchu relates to "NY-ESO-1 based therapies" is misleading, because it generalizes Batchu's teachings where Batchu itself is very specifically related only to the use of NY-ESO-1-modified DCs.

Thus, Applicant reiterates that the combination of WO 98/14464, Batchu and WO 03/076455 does not provide the skilled artisan with any reasonable expectation of success in being able to reduce the risk of relapse by administering a composition containing full length NY-ESO-1 protein and a saponin based adjuvant, as recited in the instant claims. Accordingly, this obviousness rejection is improper and should be withdrawn.

B. WO 98/14464, Batchu, WO 03/076455, Jager and U.S. 6,506,386

Claims 25, 26, 36 and 37 are rejected over the combination of WO 98/14464, Batchu WO 03/076455, Jager and U.S. 6,506,386. Applicant respectfully traverses this rejection.

In maintaining this rejection, the Advisory Action again relies on Batchu for teaching that immune responses can reduce the risk of relapse. As discussed above, however, Batchu's teachings do not go this far, and its unsupported speculations do not enable any methods of reducing the risk of relapse, let alone methods using NY-ESO-1 protein (as claimed) instead of NY-ESO-1-modified DCs.

The Advisory Action also criticizes Applicant for arguing Jager "separately," rather in view of Batchu and the other cited references. But, Jager is the only reference that uses NY-ESO-1 peptides *per se* in immunotherapeutic methods. Thus, Jager's reported results, which ***do not show any prevention of relapse***, are indeed pertinent to the pending rejection. The skilled artisan reviewing Jager, and seeing that 4/5 responsive patients ***developed additional lesions*** after vaccination with NY-ESO-1 protein, certainly would not have expected to be able to reduce the risk of relapse by administering an NY-ESO-1 protein-containing composition, as claimed. Certainly, Batchu's theoretical and speculative comments would not have overridden the expectations arising from the actual results reported in Jager.

Thus, Applicant stands by its position that the combination of WO 98/14464, Batchu, WO 03/076455, Jager and U.S. 6,506,386 does not render obvious the claimed methods. Accordingly, Applicant respectfully urges reconsideration and withdrawal of this § 103 rejection.

C. Cebon, Jager, WO 03/076455 & "the specification"

Claims 20-22, 25, 26 and 34-37 remain rejected over the combination of Cebon, Jager, WO 03/076455, Jager and an alleged "admission" in the specification regarding the patient population studied to evaluate the risk of relapse. Applicant respectfully traverses this rejection.

As explained previously, this rejection is founded on the incorrect assumption that Cebon teaches the amounts of NY-ESO-1 protein and saponin-based adjuvant recited in the claims, which it does not. Moreover, as explained above with reference to the § 102 rejection, the instant claims are even further distinguished from Cebon. Combining Cebon with Jager and WO 03/076455 fails to remedy its deficiencies. As shown above, Jager does not provide any expectation of success with regard to the ability to reduce the risk of relapse. Indeed, no combination of Cebon, Jager and WO 03/076455 provides any indication that any amount of NY-ESO-1 protein and saponin-based adjuvant would be effective to reduce the risk of relapse. Thus, this combination of references fails to establish a prima facie case of obviousness. Applicant therefore respectfully urges reconsideration and withdrawal of this § 103 rejection.

V. Unexpected Results

The Advisory Action dismisses Applicant's evidence of unexpected results for two reasons, neither of which are valid.

First, the Advisory Action alleges that "the art references shows the same result, so the result is not unexpected." This is simply not true. None of the cited references report any results showing a method that is effective to reduce the risk of relapse of an NY-ESO-1-expressing cancer, as recited in the instant claims.

- Cebon presents only initial immunological data, with ***no clinical results whatsoever***, let alone long-term results such as a reduction in relapse.
- Batchu ***speculates*** that NY-ESO-1-modified DCs might have the ***potential*** to generate CTLs that might, in turn, be effective to eliminate residual myeloma

cells responsible for relapse, but notes that results obtained to date with gene-modified DCs "are far from satisfactory." (*See* page 1341, col. 2)

- Jager reports that 4/5 responsive patients ***developed additional lesions*** after vaccination.

Thus, the results reported in Example 6 of the instant specification and in the further follow-up study reported in the Nicholaou manuscript submitted previously, showing a significant reduction in the risk of relapse, indeed are surprising and unexpected.

Second, the Advisory Action notes that "the claims do not recite that the risk of relapse is reduced for the length of time that Applicant asserts is unexpected." However, there is no requirement that the claims expressly recite the unexpected results achieved by the claimed invention in order for the unexpected results to support patentability. This issue was addressed by the Federal Circuit in a decision that is binding on the Patent Office, *In re Sullivan*, 498 F.3d 1345 (Fed. Cir. 2007) (reversing a Board decision on obviousness where the Board failed to consider evidence of unexpected results). The court explained that "[t]he issue . . . is not whether a claim ***recites*** a new use, but whether the subject matter of the claim ***possesses an unexpected use***." *Id.* at 1353 (emphasis added).

As shown previously, the claimed methods possess an unexpected use—the ability to reduce the risk of relapse of NY-ESO-1-expressing cancer. Because none of the cited references teach or suggest a method for preventing relapse of NY-ESO-1-expressing cancer, nor indicate that the claimed methods would achieve such dramatic, long-term, beneficial results in the context of preventing relapse, the results reported in the instant application and Nicholaou indeed are evidence of unexpected results that further support patentability.

For at least these reasons, Applicant respectfully urges reconsideration and withdrawal of the obviousness rejections.

VI. Request for Information Under 37 CFR § 1.105

The Advisory Action includes a Request for Information under 37 CFR § 1.105. Applicant's response to the Request for Information is provided in separate papers submitted herewith.

Applicant respectfully disagrees with the assertion that compliance with the request "cannot reasonably be considered burdensome." To the contrary, the Request is unreasonable both procedurally and substantively.

The Request is unreasonable procedurally because the Request was issued in an Advisory Action with less than 30 days remaining in the six-month statutory response period running from the February 3, 2010 final Office Action. Because the Request relates to the Cebon abstract that was first cited in the Restriction Requirement mailed February 23, 2009, Applicant believes that making this Requirement so late in prosecution without even giving applicants 30 days to respond is unreasonable.

Indeed, MPEP 704.11(b) states that "[t]he optimum time for making a requirement is ***prior to or with a first action on the merits***," and that "[o]rdinarily, a request for information ***should not be made with or after a final rejection***" (emphasis added). Moroever, MPEP 704.13 indicates that Applicant generally should be given ***at least two months***, extendable for up to six months to reply:

> Requirements for information under 37 CFR 1.105 made without an action on the merits should set a shortened statutory period of two months for reply. Applicant may extend the time period for reply up to six months in accordance with 37 CFR 1.136(a).

Thus, the requirement here violates the guidance provided by the MPEP in several respects, and hence is unreasonably burdensome on procedural grounds.

The Request is unreasonable substantively because it relates to information "discussed" at a conference that took place eight years ago. As it turns out, there was no oral presentation, so Applicant is able to identify with confidence the information that was presented. But, had there been any oral presentation, it would have been unreasonable to require Applicant to provide a statement of everything that was said eight years ago. Indeed,

the portion of the MPEP and underlying case law cited in support of the Request do not justify the requirement to provide information regarding what was presented ***orally***. MPEP 2128.01 relates to "publicly displayed documents," not oral presentations. The guidance reproduced in the Advisory Action states that "'an entirely oral presentation . . . is without question not a 'printed publication' for the purposes of 35 USC 102(b).'" Thus, there is no legal basis for the requirement to provide information on what was "discussed" at the ASCO 2002 annual meeting.

The Request also is unreasonable substantively because it requests information on "additional presentations and/or abstract presented by Applicant . . . wherein data pertinent to the subject matter was disclosed . . . " without providing any guidance on what the Examiner might deem to be "pertinent to the subject matter" and without providing any time limit on the presentations. As set forth in MPEP 704.11, "[a] requirement for information under 37 CFR 1.105 places a substantial burden on the applicant that is to be minimized by clearly focusing the reason for the requirement and the scope of the expected response." Accordingly, "the scope of the requirement should be narrowly defined." In the accompanying response, Applicant identifies all presentations of the subject matter presented in the Cebon abstract and disclosed in the application that were made prior to the September 30, 2004 filing date of the PCT application.

As noted above, despite the procedural and substantive unreasonableness of the Request, Applicant is providing a complete response thereto with this response.

Conclusion

Applicant believes that the present application is now in condition for allowance, and favorable reconsideration thereof is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment,

to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing or a credit card payment form being unsigned, providing incorrect information resulting in a rejected credit card transaction, or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date August 2, 2010 By _____

FOLEY & LARDNER LLP
Customer Number: 22428
Telephone: (202) 295-4094
Facsimile: (202) 672-5399

Courtenay C. Brinckerhoff
Attorney for Applicant
Registration No. 37,288